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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/771,383	01/25/2001	Kevin Delos Parris	2368/12	6452

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EXAMINER	
LY, CHEYNE D	
ART UNIT	PAPER NUMBER
1631	19

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/771,383	Applicant(s) PARRIS ET AL.
	Examiner Cheyne D Ly	Art Unit 1631

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 03, 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-14, 18, and 22-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-34* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *September 3, 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election without traversal of Group II which is draw to an ACPS Enzyme in Space Group R3 and an inhibitor of ACPS activity, claims15-22, in Paper No.10, filed September 3 2002, is acknowledged. Further, Applicant's request for examiner to also consider Group III, Claims 23-25, for examination. Applicant's request has been considered and it would be an undue search burden as defined by the Written Restriction Office Action, Paper 8, mailed July 2, 2002, if Group III were examined together with Group II. Therefore, the restriction requirement is still deemed proper and is therefore made FINAL.

1. Claims 18 and 22 are withdrawn because they are drawn to an activator of ACPS.

2. Claims 15-17 and 19-21 are examined on the merits.

Drawings

3. The corrected or substitute drawings were received on September 3, 2002. These drawings have been accepted. However, the corrected drawings necessitate corrections to be made to the Specification. In the Brief Description of the Figures and thereof, the references to the figures are not consistent with the figures of the corrected drawings. For example, the specification contains Figure 1 in the Brief Description of the Figures while the corrected drawing has Figures 1 and 1A-1 to 1A-107 etc.

LACK OF ENABLEMENT UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 15-17 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal structure of ACPS and ACPS-CoA complex (Example 1, Pages 22-36) and which have atom coordinates instantly disclosed (Figures 1-2A-19), does not reasonably provide enablement for a method for identifying an agent that interacts with any active site of any ACPS or any ACPS-CoA complex. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

6. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

7. It is acknowledged that the applicant has disclosed information to enable one skilled in the art to make a specific crystal of the ACPS and ACPS-CoA complex. Applicant disclosed that molecular modeling methods known in the art may be used to identify an active site of the ACPS molecule or ACPS molecular complex (Page 15, Lines 1-2). However, a method that relies on data from an unpredictable art such as protein crystallization would require clear and

precise guidance for one skilled in the art to reliably use the said method. It is well documented that protein crystallization is in essence a trial-and-error method, and the results are usually unpredictable (Drenth, J.). Accordingly, it would be very difficult for one skilled in the art to make crystal structures of other ACPS or ACPS-CoA proteins or complexes beyond the ones of the instant case where specific coordinates are disclosed. In light of the difficulty of the protein crystallization process, it is, therefore, unreasonable to expect one skilled in the art to use the information disclosed for one specific crystal to make other of predictable quality that are different from the crystal disclosed in the specification without undue experimentation.

INDEFINITENESS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

8. Claims 15-17 and 19-21 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 15-17 and 19-21 contain the abbreviation ACPS which is vague and indefinite unless accompanied by the full name, usually in parentheses.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to

the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 15-17 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosowsky et al. (1999) in view of In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983) taken with Ahern (The Scientist, 1996).

11. Rosowsky et al. (1999) discloses a method for designing based on the 3D structure of enzyme-inhibitor complexes by X-ray crystallography (Page 4854, Column 1, Lines 13-25). Molecular docking simulations for compounds into the active site were performed using the Sybyl program and recently analyzed crystals structures of the complexes were used in fitting the analogues into the active site (Page 4858, Column 2, Lines 46). Further, Rosowsky et al. discloses the inhibition of an enzyme complex by select inhibitors designed by the above method by exposing the enzyme complex to these said compounds in inhibitions assays (Page 4855, Table 1). Even though the method disclosed by Rosowsky et al. does not specify that the active sites were identified by a crystal structure coordinates and the three-dimensional model of Acyl Carrier Protein Synthetase (ACPS), the specific limitations of crystal structure coordinates and the three-dimensional model of ACPS in this instant case do not distinguish the invention from the prior art in term of patentability because they are descriptive nonfunctional subject matter.

12. In re Gulack defines nonfunctional descriptive material, as when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the invention from the prior art in term of patentability. Also, the MPEP indicates that descriptive material

that cannot exhibit any functional interrelationship with the way in which computing processes are performed does not constitute a statutory process, machine, manufacture or composition (MPEP § 2106 (IV)(B)(b)). Specific to the instant case, the coordinates data derived from crystal structures of ACPS to develop three dimensional models that are merely stored so as to be read or outputted by a computer without creating any functional interrelationship, either as part of the stored data or as part of the computing processes performed by the computer, then such descriptive material alone does not impart functionality either to the data as so structured, or to the computer.

13. The current state of the art for computational modeling makes it seemingly easy for anyone skilled in the art to apply molecular modeling programs to allow one to create approximations of a molecule's size or shape, or provide information about how a particular molecule binds to other. Many of the modeling systems currently available are easy to operate from a user's perspective, and these have essentially made it possible to perform structural determinations right at the lab bench (Ahern, Page 1, Lines 16-22). "Re-creations of the three-dimensional structure of a macromolecule such as DNA or a particular protein are, in general, derived empirically from data obtained from X-ray crystallography or nuclear magnetic resonance (NMR) spectroscopy. When X-rays are beamed into a crystallized protein, for instance, resident electrons emit secondary X-rays that scatter in all directions. This produces a distinct pattern on X-ray film, which to a casual observer resembles a series of dots arranged in concentric rings of increasing size. A crystallographer versed in interpreting these dots can transform the X-ray diffraction pattern first into an electron-density map and ultimately into a three-dimensional picture of the molecules in the crystal" (Ahern, Page 3, Lines 1-12). "Today's

molecular modeling applications run on workstations, supplanting the complex programs that once required the computing power of a mainframe. Two notable examples are SYBYL from Tripos Inc. and the Cerius² software environment from Molecular Simulations Inc. in Burlington, Mass" (Ahern, Page 3, Lines 22-25).

14. Clearly, a skilled artisan would have been motivated to partake the concept emphasized by Ahern to utilize SYBYL software for any available protein 3D determination in the inhibitor investigation type of method as in Rosowsky et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the commercially available software, Sybyl, taught by Ahern and the investigation type of method taught by Rosowsky et al. to model the crystal structure of ACPS and identify agents that interact with it.

15. Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosowsky et al. (1999) taken in view taken with Ahern (The Scientist, 1996), taken in view of Qiu et al. (1999).

16. Rosowsky et al. (1999) discloses a method for designing based on the 3D structure of enzyme-inhibitor complexes by X-ray crystallography (Page 4854, Column 1, Lines 13-25). Molecular docking simulations for compounds into the active site were performed using the Sybyl program and recently analyzed crystals structures of the complexes were used in fitting the analogues into the active site (Page 4858, Column 2, Lines 46). Further, Rosowsky et al. discloses the inhibition of an enzyme complex by select inhibitors designed by the above method by exposing the enzyme complex to these said compounds in inhibitions assays (Page 4855, Table 1). However, the method disclosed by Rosowsky et al. does not specify that the active

sites were identified by a crystal structure coordinates and the three-dimensional model of Acyl Carrier Protein Synthetase (ACPS).

17. The current state of the art for computational modeling makes it seemingly easy for anyone skilled in the art to apply molecular modeling programs to allow one to create approximations of a molecule's size or shape, or provide information about how a particular molecule binds to other. Many of the modeling systems currently available are easy to operate from a user's perspective, and these have essentially made it possible to perform structural determinations right at the lab bench (Ahern, Page 1, Lines 16-22). "Re-creations of the three-dimensional structure of a macromolecule such as DNA or a particular protein are, in general, derived empirically from data obtained from X-ray crystallography or nuclear magnetic resonance (NMR) spectroscopy. When X-rays are beamed into a crystallized protein, for instance, resident electrons emit secondary X-rays that scatter in all directions. This produces a distinct pattern on X-ray film, which to a casual observer resembles a series of dots arranged in concentric rings of increasing size. A crystallographer versed in interpreting these dots can transform the X-ray diffraction pattern first into an electron-density map and ultimately into a three-dimensional picture of the molecules in the crystal" (Ahern, Page 3, Lines 1-12). "Today's molecular modeling applications run on workstations, supplanting the complex programs that once required the computing power of a mainframe. Two notable examples are SYBYL from Tripos Inc. and the Cerius² software environment from Molecular Simulations Inc. in Burlington, Mass" (Ahern, Page 3, Lines 22-25).

18. Qiu et al. discloses the crystal structure for β-Ketoacyl-acyl carrier synthase III (FabH). The crystal structures of FabH were determined in the presence and absence of acetyl-CoA (Page 36465, Lines 1-6).

19. Clearly, a skilled artisan would have been motivated to partake the concept emphasized by Ahern to utilize SYBYL software for any available protein 3D determination in the inhibitor investigation type of method as in Rosowsky et al. and apply such method to the crystal structure for β-Ketoacyl-acyl carrier synthase III (FabH) disclosed by Qiu et al. for identifying agents that interact with ACPS. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the commercially available software, Sybyl, taught by Ahern and the investigation type of method taught by Rosowsky et al. with the β-Ketoacyl-acyl carrier synthase III (FabH) disclosed by Qiu et al to identify agents that interact with ACPS base on 3D coordinate data.

20. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

22. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

23. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
12/2/02

ARDIN H. MARSCHEL
PRIMARY EXAMINER